A10

125. (Amended) Use according to claim 124, where one of the target genes is the PKR gene.

REMARKS

The application has been amended to conform to U.S. practice. The claims have been amended to eliminate multiple dependency.

STATEMENT UNDER 37 CFR 1.821(f)

I, John P. Murtaugh, hereby state that the information recorded in computer readable form is identical to the written sequence listing.

Please charge any fees and credit any overpayments under 37 CFR 1. 16 and 1. 17 during the entire pendency of this application to our Deposit Account No. 16-0820, Order No. 33796.

If any fees are required by this communication, please charge such fees to our Deposit Account No. 16-0820, Order No. 33796.

Respectfully submitted,

PEARNE & GORDON LLP

By John P. Murtaugh

John P. Murtaugh. Reg. No. 34226

526 Superior Avenue East
Suite 1200
Cleveland, Ohio 44114-1484
(216) 579-1700

Date: 7-20-01

INDICATION OF REVISIONS TO THE CLAIMS
IN U.S. NATIONAL PHASE OF PCT/DE00/00244

3. (Amended) Method according to [either of the preceding claims] claim 1, where the dsRNA is enclosed by natural viral capsids or by chemically or enzymatically produced artificial capsids or structures derived therefrom.

4. (Amended) Method according to [one of the preceding claims] claim 1, where the target gene is expressed in eukaryotic cells.

5. (Amended) Method according to [one of the preceding claims] claim 1, where the target gene is selected from the following group: oncogene, cytokin gene, Id-protein gene, development gene, prion gene.

6. (Amended) Method according to [one of the preceding claims] claim 1, where the target gene is expressed in pathogenic organisms, preferably in plasmodia.

7. (Amended) Method according to [one of the preceding claims] claim 1, where the target gene is part of a virus or viroid.

10. (Amended) Method according to [one of the preceding claims] claim 1, where segments of the dsRNA are in double-stranded form.

11. (Amended) Method according to [one of the preceding claims] claim 1, where the ends of the dsRNA are modified in order to counteract degradation in the cell or dissociation into the single strands.

12. (Amended) Method according to [one of the preceding claims] claim 1, where the cohesion of the double-stranded structure, which is caused by the complementary nucleotide

pairs, is increased by at least one, preferably two, further chemical linkage(s).

13. (Amended) Method according to [one of the preceding claims] claim 1, where the chemical linkage is formed by a covalent or ionic bond, a hydrogen bond, hydrophobic interactions, preferably van-der-Waals or stacking interactions, or by metal-ion coordination.

14. (Amended) Method according to [one of the preceding claims] claim 1, where the chemical linkage is generated at at least one, preferably both, ends of the double-stranded structure.

15. (Amended) Method according to [one of the preceding claims] claim 1, where the chemical linkage is formed by means of one or more compound groups, the compound groups preferably being poly(oxyphosphinicooxy-1,3-propanediol) and/or polyethylene glycol chains.

16. (Amended) Method according to [one of the preceding claims] claim 1, where the chemical linkage is formed by purine analogs used in the double-stranded structure in place of purines.

17. (Amended) Method according to [one of the preceding claims] claim 1, where the chemical linkage is formed by azabenzene units introduced into the double-stranded structure.

18. (Amended) Method according to [one of the preceding claims] claim 1, where the chemical linkage is formed by branched nucleotide analogs used in the double-stranded structure in place of nucleotides.

19. (Amended) Method according to [one of the preceding claims] claim 1, where at least one of the following groups is used for generating the chemical linkage: methylene blue; bifunctional groups, preferably bis(2-chloroethyl)amine; N-acetyl-N'-(p-glyoxylbenzoyl)cystamine; 4-thiouracil; psoralene.

20. (Amended) Method according to [one of the preceding claims] claim 1, where the

chemical linkage is formed by thiophosphoryl groups provided at the ends of the double-stranded structure.

21. (Amended) Method according to [one of the preceding claims] claim 1, where the chemical linkage at the ends of the double-stranded structure is formed by triple-helix bonds.

22. (Amended) Method according to [one of the preceding claims] claim 1, where at least one 2'-hydroxyl group of the nucleotides of the dsRNA in the double-stranded structure is replaced by a chemical group, preferably a 2'-amino or a 2'-methyl group.

23. (Amended) Method according to [one of the preceding claims] claim 1, where at least one nucleotide in at least one strand of the double-stranded structure is a locked nucleotide with a sugar ring which is chemically modified, preferably by a 2'-O, 4'-C-methylene bridge.

24. (Amended) Method according to [one of the preceding claims] claim 1, where the dsRNA is bound to, associated with or surrounded by, at least one viral coat protein which originates from a virus, is derived therefrom or has been prepared synthetically.

25. (Amended) Method according to [one of the preceding claims] claim 1, where the coat protein is derived from polyomavirus.

26. (Amended) Method according to [one of the preceding claims] claim 1, where the coat protein contains the polyomavirus virus protein 1 (VP1) and/or virus protein 2 (VP2).

27. (Amended) Method according to [one of the preceding claims] claim 1, where, when a capsid or capsid-type structure is formed from the coat protein, one side faces the interior of the capsid or capsid-type structure.

28. (Amended) Method according to [one of the preceding claims] claim 1, where one strand of the dsRNA is complementary to the primary or processed RNA transcript of the target gene.

29. (Amended) Method according to [one of the preceding claims] claim 1, where the cell is a vertebrate cell or a human cell.

30. (Amended) Method according to [one of the preceding claims] claim 1, where at least two dsRNAs which differ from each other are introduced into the cell, where at least segments of one strand of each dsRNA are complementary to in each case one of at least two different target genes.

31. (Amended) Method according to [one of the preceding claims] claim 1, where one of the target genes is the PKR gene.

34. (Amended) Medicament according to [either of claims 32 or 33] claim 32, where the dsRNA is enclosed by natural viral capsids or by chemically or enzymatically produced artificial capsids or structures derived therefrom.

35. (Amended) Medicament according to [one of claims 32 to 34] claim 32, where the target gene can be expressed in eukaryotic cells.

36. (Amended) Medicament according to [one of claims 32 to 35] claim 32, where the target gene is selected from the following group: oncogene, cytokin gene, Id-protein gene, development gene, prion gene.

37. (Amended) Medicament according to [one of claims 32 to 36] claim 32, where the target gene can be expressed in pathogenic organisms, preferably in plasmodia.

38. (Amended) Medicament according to [one of claims 32 to 37] claim32, where the target gene is part of a virus or viroid.

41. (Amended) Medicament according to [one of claims 32 to 40] claim 32, where segments of the dsRNA are in double-stranded form.

42. (Amended) Medicament according to [one of claims 32 to 40] claim 32, where the

ends of the dsRNA are modified in order to counteract degradation in the cell or dissociation into the single strands.

43. (Amended) Medicament according to [one of claims 32 to 42] claim 32, where the cohesion of the double-stranded structure, which is caused by the complementary nucleotide pairs, is increased by at least one, preferably two, further chemical linkage(s).

44. (Amended) Medicament according to [one of claims 32 to 43] claim 32, where the chemical linkage is formed by a covalent or ionic bond, a hydrogen bond, hydrophobic interactions, preferably van-der-Waals or stacking interactions, or by metal-ion coordination.

45. (Amended) Medicament according to [one of claims 32 to 44] claim 32, where the chemical linkage is generated at at least one, preferably both, ends of the double-stranded structure.

46. (Amended) Medicament according to [one of claims 32 to 45] claim 32, where the chemical linkage is formed by means of one or more compound groups, the compound groups preferably being poly(oxyphosphinicooxy-1,3-propanediol) and/or polyethylene glycol chains.

47. (Amended) Medicament according to [one of claims 32 to 46] claim 32, where the chemical linkage is formed by purine analogs used in the double-stranded structure in place of purines.

48. (Amended) Medicament according to [one of claims 32 to 47] claim 32, where the chemical linkage is formed by azabenzene units inserted into the double-stranded structure.

49. (Amended) Medicament according to [one of claims 32 to 48] claim 32, where the chemical linkage is formed by branched nucleotide analogs used in the double-stranded structure in place of nucleotides.

50. (Amended) Medicament according to [one of claims 32 to 49] claim 32, where at

least one of the following groups is used for generating the chemical linkage: methylene blue; bifunctional groups, preferably bis(2-chloroethyl)amine; N-acetyl-N'-(p-glyoxylbenzoyl)cystamine; 4-thiouracil; psoralene.

51. (Amended) Medicament according to [one of claims 32 to 50] claim 32, where the chemical linkage is formed by thiophosphoryl groups provided at the ends of the double-stranded structure.

52. (Amended) Medicament according to [one of claims 32 to 51] claim 32, where the chemical linkage are [sic] triple-helix bonds provided at the ends of the double-stranded structure.

53. (Amended) Medicament according to [one of claims 32 to 52] claim 32, where at least one 2'-hydroxyl group of the nucleotides of the dsRNA in the double-stranded structure is replaced by a chemical group, preferably a 2'-amino or a 2'-methyl group.

54. (Amended) Medicament according to [one of claims 32 to 53] claim 32, where at least one nucleotide in at least one strand of the double-stranded structure is a locked nucleotide with a sugar ring which is chemically modified, preferably by a 2'-O, 4'-C-methylene bridge.

55. (Amended) Medicament according to [one of claims 32 to 54] claim 32, where the dsRNA is bound to, associated with or surrounded by, at least one viral coat protein which originates from a virus, is derived therefrom or has been prepared synthetically.

56. (Amended) Medicament according to [one of claims 32 to 55] claim 32, where the coat protein is derived from the polyomavirus.

57. (Amended) Medicament according to [one of claims 32 to 56] claim 32, where the coat protein contains the polyomavirus virus protein 1 (VP1) and/or virus protein 2 (VP2).

58. (Amended) Medicament according to [one of claims 32 to 57] claim 32, where, when a capsid or capsid-type structure is formed from the coat protein, one side faces the interior of

the capsid or capsid-type structure.

59. (Amended) Medicament according to [one of claims 32 to 58] claim 32, where one strand of the dsRNA is complementary to the primary or processed RNA transcript of the target gene.

60. (Amended) Medicament according to [one of claims 32 to 59] claim 32, where the cell is a vertebrate cell or a human cell.

61. (Amended) Medicament according to [one of claims 32 to 60] claim 32, where at least two dsRNAs which differ from each other are contained in the medicament, where at least segments of one strand of each dsRNA are complementary to in each case one of at least two different target genes.

65. (Amended) Active ingredient according to claim 63 [or 64], where segments of the dsRNA are in double-stranded form.

66. (Amended) Active ingredient according to [one of claims 63 to 65] claim 63, where the ends of the dsRNA are modified in order to counteract degradation in the cell or dissociation into the single strands.

67. (Amended) Active ingredient according to [one of claims 63 to 66] claim 63, where the cohesion of the double-stranded structure, which is caused by the complementary nucleotide pairs, is increased by at least one, preferably two, further chemical linkage(s).

68. (Amended) Active ingredient according to [one of claims 63 to 67] claim 63, where the chemical linkage is formed by a covalent or ionic bond, a hydrogen bond, hydrophobic interactions, preferably van-der-Waals or stacking interactions, or by metal-ion coordination.

69. (Amended) Active ingredient according to [one of claims 63 to 68] claim 63, where the chemical linkage is generated at at least one, preferably both, ends of the double-stranded structure.

70. (Amended) Active ingredient according to [one of claims 63 to 69] claim 63, where the chemical linkage is formed by means of one or more compound groups, the compound groups preferably being poly(oxyphosphinicooxy-1,3-propanediol) and/or polyethylene glycol chains.

71. (Amended) Active ingredient according to [one of claims 63 to 70] claim 63, where the chemical linkage is formed by purine analogs used in the double-stranded structure in place of purines.

72. (Amended) Active ingredient according to [one of claims 63 to 71] claim 63, where the chemical linkage is formed by azabenzene units inserted into the double-stranded structure.

73. (Amended) Active ingredient according to [one of claims 63 to 72] claim 63, where the chemical linkage is formed by branched nucleotide analogs used in the double-stranded structure in place of nucleotides.

74. (Amended) Active ingredient according to [one of claims 63 to 73] claim 63, where at least one of the following groups is used for generating the chemical linkage: methylene blue; bifunctional groups, preferably bis(2-chloroethyl)amine; N-acetyl-N'-(p-glyoxylbenzoyl)cystamine; 4-thiouracil; psoralene.

75. (Amended) Active ingredient according to [one of claims 63 to 74] claim 63, where the chemical linkage is formed by thiophosphoryl groups provided at the ends of the double-stranded structure.

76. (Amended) Active ingredient according to [one of claims 63 to 75] claim 63, where the chemical linkage are triple-helix bonds provided at the ends of the double-stranded structure.

77. (Amended) Active ingredient according to [one of claims 63 to 76] claim 63, where at

least one 2'-hydroxyl group of the nucleotides of the dsRNA in the double-stranded structure is replaced by a chemical group, preferably a 2'-amino or a 2'-methyl group.

78. (Amended) Active ingredient according to [one of claims 63 to 77] claim 63, where at least one nucleotides at least one strand of the double-stranded structure is a locked nucleotide with a sugar ring which is chemically modified, preferably by a 2'-O, 4'-C-methylene bridge.

79. (Amended) Active ingredient according to [one of claims 63 to 78] claim 63, where one strand of the dsRNA is complementary to the primary or processed RNA transcript of the target gene.

80. (Amended) Active ingredient according to [one of claims 63 to 79] claim 63, where at least two dsRNAs which differ from each other are contained in the active ingredient, where at least segments of one strand of each dsRNA are complementary to in each case one of at least two different target genes.

83. (Amended) Use according to [either of claims 81 or 82] claim 81, where the dsRNA is enclosed by natural viral capsids or by chemically or enzymatically produced artificial capsids or structures derived therefrom.

84. (Amended) Use according to [one of claims 81 to 83] claim 81, where the target gene can be expressed in eukaryotic cells.

85. (Amended) Use according to [one of claims 81 to 84] claim 81, where the target gene is selected from the following group: oncogene, cytokin gene, Id-protein gene, development gene, prion gene.

86. (Amended) Use according to [one of claims 81 to 85] claim 81, where the target gene can be expressed in pathogenic organisms, preferably in plasmodia.

87. (Amended) Use according to [one of claims 81 to 86] claim 81, where the target gene is part of a virus or viroid.

90. (Amended) Use according to [one of claims 81 to 89] claim 81, where segments of the dsRNA are in double-stranded form.

91. (Amended) Use according to [one of claims 81 to 90] claim 81, where the ends of the dsRNA are modified in order to counteract degradation in the cell or dissociation into the single strands.

92. (Amended) Use according to [one of claims 81 to 91] claim 81, where the cohesion of the double-stranded structure, which is caused by the complementary nucleotide pairs, is increased by at least one, preferably two, further chemical linkage(s).

93. (Amended) Use according to [one of claims 81 to 92] claim 81, where the chemical linkage is formed by a covalent or ionic bond, a hydrogen bond, hydrophobic interactions, preferably van-der-Waals or stacking interactions, or by metal-ion coordination.

94. (Amended) Use according to [one of claims 81 to 93] claim 81, where the chemical linkage is generated at at least one, preferably both, ends of the double-stranded structure.

95. (Amended) Use according to [one of claims 81 to 94] claim 81, where the chemical linkage is formed by means of one or more compound groups, the compound groups preferably being poly(oxyphosphinicooxy-1,3-propanediol) and/or polyethylene glycol chains.

96. (Amended) Use according to [one of claims 81 to 95] claim 81, where the chemical linkage is formed by purine analogs used in the double-stranded structure in place of purines.

97. (Amended) Use according to [one of claims 81 to 96] claim 81, where the chemical linkage is formed by azabenzene units introduced into the double-stranded structure.

98. (Amended) Use according to [one of claims 81 to 97] claim 81, where the chemical linkage is formed by branched nucleotide analogs used in the double-stranded structure in place of nucleotides.

99. (Amended) Use according to [one of claims 81 to 98] claim 81, where at least one of the following groups is used for generating the chemical linkage: methylene blue; bifunctional groups, preferably bis(2-chloroethyl)amine; N-acetyl-N'-(p-glyoxylbenzoyl)cystamine; 4-thiouracil; psoralene.

100. (Amended) Use according to [one of claims 81 to 99] claim 81, where the chemical linkage is formed by thiophosphoryl groups attached to the ends of the double-stranded structure.

101. (Amended) Use according to [one of claims 81 to 100] claim 81, where the chemical linkage at the ends of the double-stranded structure is formed by triple-helix bonds.

102. (Amended) Use according to [one of claims 81 to 101] claim 81, where at least one 2'-hydroxyl group of the nucleotides of the dsRNA in the double-stranded structure is replaced by a chemical group, preferably a 2'-amino or a 2'-methyl group.

103. (Amended) Use according to [one of claims 81 to 102] claim 81, where at least one nucleotide in at least one strand of the double-stranded structure is a locked nucleotide with a sugar ring which is chemically modified, preferably by a 2'-O, 4'-C-methylene bridge.

104. (Amended) Use according to [one of claims 81 to 103] claim 81, where the dsRNA is bound to, associated with or surrounded by, at least one viral coat protein which originates from a virus, is derived therefrom or has been prepared synthetically.

105. (Amended) Use according to [one of claims 81 to 104] claim 81, where the coat protein is derived from polyomavirus.

106. (Amended) Use according to [one of claims 81 to 105] claim 81, where the coat

protein contains the polyomavirus virus protein 1 (VP1) and/or virus protein 2 (VP2).

107. (Amended) Use according to [one of claims 81 to 106] claim 81, where, when a capsid or capsid-type structure is formed from the coat protein, one side faces the interior of the capsid or capsid-type structure.

108. (Amended) Use according to [one of claims 81 to 107] claim 81, where one strand of the dsRNA is complementary to the primary or processed RNA transcript of the target gene.

109. (Amended) Use according to [one of claims 81 to 108] claim 81, where the cell is a vertebrate cell or a human cell.

110. (Amended) Use according to [one of claims 81 to 109] claim 81, where at least two dsRNAs which differ from each other are used, where at least segments of one strand of each dsRNA are complementary to in each case one of at least two different target genes.

112. (Amended) Use according to [one of claims 81 to 111] claim 81, where the medicament is injectable into the blood-stream or into the interstitium of the organism to undergo therapy.

113. (Amended) Use according to [one of claims 81 to 112] claim 81, where the dsRNA is taken up into bacteria or micro-organisms.

116. (Amended) Use according to claim 114 [or 115], where the target gene is selected from the following group: oncogene, cytokin gene, Id-protein gene, development gene, prion gene.

117. (Amended) Use according to [one of claims 114 to 116] claim 114, where the target gene can be expressed in patho-genic organisms, preferably in plasmodia.

118. (Amended) Use according to [one of claims 114 to 117] claim 114, where the target gene is part of a virus or viroid.

121. (Amended) Use according to [one of claims 114 to 120] claim 114, where segments of the dsRNA are in double-stranded form.

122. (Amended) Use according to [one of claims 114 to 121] claim 114, where one strand of the dsRNA is complementary to the primary or processed RNA transcript of the target gene.

123. (Amended) Use according to [one of claims 114 to 122] claim 114, where the cell is a vertebrate cell or a human cell.

124. (Amended) Use according to [one of claims 114 to 123] claim 114, where at least two dsRNAs which differ from each other are used, where at least segments of one strand of each dsRNA are complementary to in each case one of at least two different target genes.

125. (Amended) Use according to claim [125] 124, where one of the target genes is the PKR gene.